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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,409	10/13/2004	Xia Xu	4239-64801-02	9192
45160 7590 10/23/2009 WOODCOCK WASHBURN LLP CIRA CENTRE, 12TH FLOOR 2929 ARCH STREET PHILADELPHIA, PA 19104-2891				
EXAMINER				
FRITCHMAN, REBECCA M				
ART UNIT		PAPER NUMBER		
1797				
MAIL DATE		DELIVERY MODE		
10/23/2009		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/511,409

**Applicant(s)**

XU ET AL.

**Examiner**

REBECCA FRITCHMAN

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 June 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/ICE)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

***Detailed Action  
Summary***

1. This is Final Office action based on 10/511409 application attorneys remarks filed on 06/22/2009.
2. Claims 1-18 are pending and have been fully considered.

***Claim Rejections - 35 USC § 103***

**3. Claims 1-9, 12-14, & 16-18 are rejected under 35 U.S.C. 103(a) as being obvious over VISSER et al.(High-performance liquid chromatography of the neuroactive steroids alphaxalone and prefnanolone in plasma using dansyl hydrazine as fluorescent label: application to pharmacokinetic-pharmacodynamic study in rats, J Chrom B, vol. 745, pgs. 357-363(2000)) in view of Bailey et al.(USP 5807748), and in further view of TAKADATE et al. in (A Convenient Derivatization with Anion Exchange Resin Catalysts for High-Performance Liquid Chromatographic Analysis. I. Derivatization of Estrogens with Dansyl Chloride, Chem. Pharm. Bull., vol. 33, no. 11, pages 5092-5095(1985)).**

VISSER et al. teaches of reacting a sample with a sulfohydrazine to form a sulfonylhydrazone of a ketosteroid (Figure 1) and analyzing the reacted sample by high-performance liquid chromatography (abstract), wherein detection of the sulfonylhydrazone indicates presence of the ketosteroid (Section 3). The non-polar phase is a C18 stationary phase (Section2) A methanol/water solvent is used during the HPLC (Section 2).

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VISSER et al. does not teach of analyzing the reacted sample by mass spectrometry. BAILEY et al. teach of using reversed phase HPLC and electrospray mass spectrometry for separating and identifying a fluorescent derivative of an analyte molecule (Columns 1-4, examples). Bailey et al. teaches that the disclosed method improves sensitivity (column 4). Therefore, it would have been obvious to one of ordinary skill in the art to modify the method of VISSER et al with the separation and identification techniques of BAILEY et al. in order to gain the advantages of improved detection sensitivity.

VISSER and BAILEY et al. do not teach of using a sulfonyl halide following using the sulfonylhydrazide. TAKADATE et al. teach that derivatization of ketosteroid estrogens using a sulfonyl halide is an alternative derivatization to that of ketosteroids using sulfonylhydrazides. It would have been obvious to one of ordinary skill in the analytical chemistry arts to follow the derivatization of ketosteroids using sulfonylhydrazides with an alternative and well-known method of derivatization of ketosteroids using sulfonyl halide. The purpose or advantage of doing so would be to check the relative accuracy of the first method. Thus, it would have been obvious for one of ordinary skill in the art to follow the sulfonylhydrazide reaction with a sulfonyl halide reaction to gain the advantages of comparison testing.

**4. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being obvious over BERLINER in US 5272134 in view of Bailey in US 5807748, and in further view of TAKADATE et al. in (A Convenient Derivatization with Anion**

**Exchange Resin Catalysts for High-Performance Liquid Chromatographic Analysis. I. Derivatization of Estrogens with Dansyl Chloride, Chem. Pharm. Bull., vol. 33, no. 11, pages 5092-5095(1985)).**

BERLINER teaches of reacting a sample with sulfonylhydrazide to form a sulfonylhydrazone of a ketosteroid in the sample and analyzing the reacted sample (Example 13-15). Berliner teaches that using methanol washes the product clean (Examples 13-15) and teaches using the methanol/water elution ratio 80:20(examples 13-15).

BERLINER does not expressly teach the method of analysis used. BAILEY et al. teach of using reversed phase HPLC and electrospray mass spectrometry for separating and identifying a fluorescent derivative of an analyte molecule (Columns 1-4, examples). Bailey et al. teaches that the disclosed method improves sensitivity (column 4). Therefore, it would have been obvious to one of ordinary skill in the art to modify the method of BERLINER et al with the separation and identification techniques of BAILEY et al. in order to gain the advantages of improved detection sensitivity.

BERLINER and BAILEY et al. do not teach of using a sulfonyl halide following using the sulfonylhydrazide. TAKADATE et al. teach that derivatization of ketosteroid estrogens using a sulfonyl halide is an alternative derivatization to that of ketosteroids using sulfonylhydrazides. It would have been obvious to one of ordinary skill in the analytical chemistry arts to follow the derivatization of ketosteroids using sulfonylhydrazides with an alternative and well-known method of derivatization of ketosteroids using sulfonyl halide. The purpose or advantage

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of doing so would be to check the relative accuracy of the first method. Thus, it would have been obvious for one of ordinary skill in the art to follow the sulfonhydrazide reaction with a sulfonyl halide reaction to gain the advantages of comparison testing.

### ***Response to Arguments***

Applicant's arguments filed 06/22/2009 have been fully considered but they are not persuasive.

In response to applicant's argument that the examiners reasoning for combination (with TAKADATE) is different than the applicants, which is that, " the two-step process of carbonyl derivatization followed by hydroxyl derivatization provides for better HPLC separation of steroids, and allows for better signal detection in API-MS", the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is

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filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to REBECCA FRITCHMAN whose telephone number is (571)270-5542. The examiner can normally be reached on Monday-Friday 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kim, Vickie can be reached on 571-272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Krishnan S Menon/  
Primary Examiner, Art Unit 1797

R.F.